

## REMARKS

### Discussion of Abstract, Specification and Claim Amendments

The Abstract is amended to correct a typographical error so that “raf” instead of “ras” is recited. This amendment better reflects the claims, which are supported by the disclosure as filed on Page 15, line 27 and Examples 1-8.

The specification is amended to delete “Anti” from the heading to Example 6.

Claims 2-9 and 12-20 are amended to improve their syntax and/or grammar.

Claim 1 has been amended to more distinctly claim the present invention. This amendment is supported by the specification as filed on Page 5, line 13. New claim 23 is supported by the disclosure as filed on page 4, line 26, to page 5, line 2. In addition, Claims 10 and 11 have been canceled. Accordingly, no new matter is added by way of these amendments.

### The Office Action

The Office Action objects to the term “Anti Chemotherapeutic” in the specification as filed, on page 43, line 16. The Office Action also rejects claim 9 for misspelling “phosphothiorated.”

The Office Action alleges that the specification does not enable a person skilled in the art to make and use the full scope of the present invention without undue experimentation, and that claims 1-8 and 12-22 lack adequate written description in the application as filed.

In addition, the Office Action alleges that the present invention is patentably indistinct from the invention claimed in US Patent 6,126,965.

### The Present Invention

The present invention relates to a method of chemosensitizing tumor tissue by using a cationic liposomal composition containing at least one oligonucleotide that binds to a raf oncogene expressed by the tumor.

### Discussion of Rejections Based on Formalities

The Office Action objects to the term “Anti Chemotherapeutic” in the specification as filed, on page 43, line 16. The Office Action also rejects claim 9 for misspelling “phosphothiorated.” The description and claims have been amended to address these allegations.

### **Discussion of Enablement and Written Description Rejections under Section 112**

Firstly, the Office Action alleges that the claims fail to comply with Section 112 because the disclosure fails to enable a skilled artisan to make the composition. Similarly, the Office Action alleges that the alleged failure of the specification to list a representative number of species in each genus encompassed by the claims allegedly shows that the applicants were not in possession of the claimed invention as of the filing date. In this regard, the Office Action suggests that the specification and claims do not distinguish the elements that are essential to the genera comprising “an oligonucleotide, an anti-metabolite, a natural product, a hormone, an antagonist, a substituted urea, a methylhydrazine derivative, a small molecule inhibitor, peptide or antibody.” Applicants respectfully request reconsideration for the following reasons. As amended, the present invention distinctly claims the formulation of liposomal raf antisense oligonucleotides (as described in Examples 1-8) and one or more chemotherapeutic agents. For the chemotherapeutic agents, a skilled artisan would know that “an anti-metabolite, a natural product, a hormone, an antagonist, a substituted urea, a methylhydrazine derivative, a small molecule inhibitor, peptide or antibody” represent different chemotherapeutic agents that are administered depending on the cancer to be treated (*See Physician’s Desk Reference*, 2000 and 2001). Thus, the disclosure enables a skilled artisan to make the claimed composition.

Secondly, the Office Action alleges that the present invention fails to comply with Section 112 because the disclosure fails to enable the method of chemosensitizing tumor tissue (for any oligonucleotide). The Office Action acknowledges that the specification and claims enable the enhanced delivery of SEQ ID NO:1 and mitoxantrone but do not enable the chemosensitization using *any* antisense oligonucleotide and chemotherapeutic agent. Applicants respectfully request reconsideration for the following reasons. As amended, the present invention distinctly claims the administration of raf antisense oligonucleotides whereby such administration leads to the chemosensitization of tumor tissue (*See Examples 4-8*). Thus, the disclosure enables a skilled artisan to use the method as claimed.

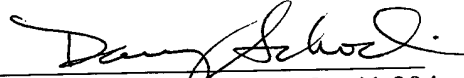
### **Discussion of Double Patenting over U.S. Patent No. 6,126,965**

The Office Action alleges that claims 10 and 11, of the present invention, are patentably indistinct over US 6,126,965 (‘965). Claims 10 and 11 have been canceled. Accordingly, the presently claimed invention is patentably distinct from ‘965.

**Conclusion**

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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